Cluster of Serogroup C Meningococcal Disease Associated With Attendance at a Party

REBECCA FINN, MD, Pittsburgh, Pa; CARMELA GROVES, RN, MS, Baltimore, Md; MELANIE COE, RN, La Plata, Md; MARGARET PASS, MS, CIC, Baltimore, Md; and LEE H. HARRISON, MD, Pittsburgh, Pa

ABSTRACT

Background. An unexplained increase has occurred in the incidence of invasive meningococcal disease in adolescents and young adults.

Methods. We investigated a cluster of serogroup C meningococcal disease in 3 previously healthy young adults who had attended a party in Maryland. Molecular subtyping was done on the isolates from the 3 cluster cases and 4 control isolates by pulsed-field gel electrophoresis (PFGE). The only common exposure was attendance at the party, where a large number of people reportedly smoked tobacco or marijuana and/or drank alcohol.

Results. The PFGE analysis of the 3 case isolates showed identical molecular subtypes.

Conclusion. This investigation strongly suggests that transmission of the cluster strain occurred at the party. Transmission may have occurred in part as a result of the recently described risk factors of binge drinking and smoking. Taken together, these findings suggest that some of the recent increase in invasive meningococcal disease may be due to modifiable risk factors.

NEISSERIA MENINGITIDIS is a major cause of invasive bacterial infections, including meningitis.[1] In recent years, the overall annual incidence of meningococcal infection in the United States has been about 1.0 per 100,000 population.[2] Adolescents and young adults have typically had a low risk of invasive meningococcal infection. During the 1990s, there was a substantial increase in the incidence of meningococcal disease in adolescents and young adults.[3-5] We present a cluster of meningococcal infections associated with a party, which raises interesting points about the changing epidemiology of meningococcal infection in this age group.

CASE REPORTS

Case 1. An 18-year-old healthy male laborer had headache, fever, nausea, and vomiting on May 19, 1999. On May 20, he went to a local emergency department, where he had cardiopulmonary arrest. He was transported to a tertiary care hospital by air and was pronounced dead on arrival. His mother noticed that he had a fine rash when she saw him shortly after death. Blood cultures obtained before death grew *Neisseria meningitidis*. Cerebrospinal fluid was not obtained. This patient reportedly smoked 2 to 3 cigarettes per day and drank an average of 2 to 4 beers per week.

Case 2. A 20-year-old healthy male plumbing company worker went to the hospital with headache and back pain on May 21, 1999. On admission, he had a temperature of 38.9°C and appeared severely ill and lethargic. He was noted to have an erythematous rash on his forehead, arms, and lower extremities. Blood cultures obtained on admission were positive for *N meningitidis,* and culture of the cerebrospinal fluid was negative. He responded rapidly to antibiotic therapy and was discharged. He reportedly smoked 1 to 1½ packs of cigarettes per day and drank 2 to 4 beers per week.

Case 3. A 21-year-old man who worked part-time at a restaurant went to a hospital emergency department on May 25, 1999, with headache, neck pain, vomiting, and hypotension. Blood cultures taken on the date of admission were positive for *N meningitidis;* culture of the cerebrospinal fluid was negative. He was treated successfully and discharged from the hospital. He reportedly smoked 1 to 1½ packs of cigarettes per day; information on his drinking habits was not available.

KEY POINTS

- The risk of meningococcal infection recently increased in adolescents and young adults.
- Certain behaviors, such as bar patronage, binge drinking, and cigarette smoking are recently identified risk factors for meningococcal infection.
- We investigated an outbreak of meningococcal infection associated with a party.
- All party-related meningococcal strains had identical DNA fingerprints.
- Transmission most likely occurred at the party.

From the Infectious Diseases Epidemiology Research Unit, Departments of Epidemiology and Medicine, University of Pittsburgh Graduate School of Public Health and School of Medicine, Pittsburgh, Pa; the Epidemiology and Disease Control Program, Community and Public Health Administration, Maryland Department of Health and Mental Hygiene, Baltimore; the Charles County Health Department, La Plata, Md; and the Department of International Health, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Md.

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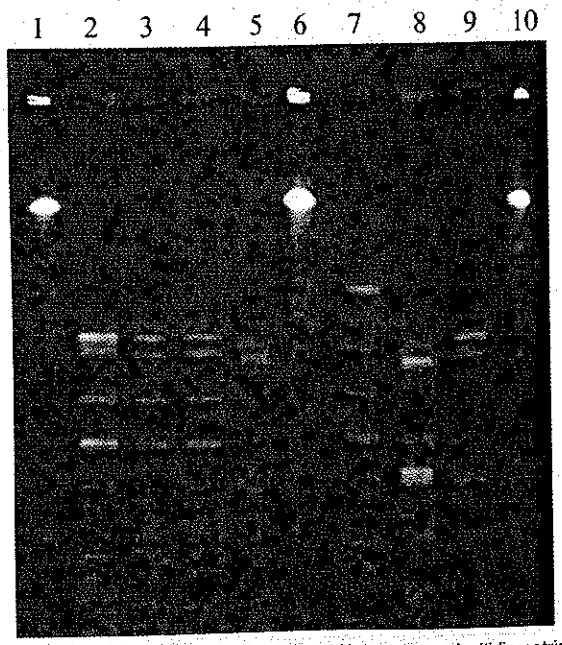
Reprint requests to Lee H. Harrison, MD, University of Pittsburgh Graduate School of Public Health, Department of Epidemiology, 521 Parran Hall, 130 DeSoto St, Pittsburgh, PA 15261.

EPIDEMIOLOGIC AND MICROBIOLOGIC INVESTIGATIONS

This outbreak was identified by routine public health surveillance. Investigation of this outbreak included review of medical records and interviews with persons associated with the case patients.

Species confirmation and serogroup determination were done using standard methods.[6] Molecular subtyping was done by PFGE as previously described.[7] Briefly, the meningococcal isolates were stored at –70°C in trypticase soy broth with 30% glycerol and subcultured on chocolate agar at 37°C in a 5% CO_2 incubator. The cells were suspended in tris-EDTA (TE) 1X buffer to achieve an optical density of about 1.8. An equal volume of the suspension was mixed with 2% Seaplaque agarose, pipetted into a plug mold, and allowed to solidify. The plugs were placed in a lysozyme lysis buffer solution at 37°C overnight. The next day the lysozyme lysis buffer was replaced with 1 mg/mL proteinase K (EDTA, Sarkosyl, proteinase K) buffer, and then placed in a 50°C bath for 3 hours. The plugs were then washed four times with TE buffer, washed twice with the appropriate restriction endonuclease buffer, and incubated overnight with the appropriate restriction enzyme. Three endonucleases (*Nhe*I, *Sfi*I, and *Spe*I) were used to obtain a genetic fingerprint pattern for each of the isolates. A 1% agarose gel was made and poured into a mold with the slots into which the plugs were placed, and then sealed into place with agarose. The gel was then placed in the clamped homologous electric fields DR-3 III PFGE apparatus (Bio-Rad Laboratories, Hercules, Calif), and was run with switch times of 1 to 30 seconds for 24 hours, at 6 volts per minute. Molecular subtyping was done on the three cluster isolates, in addition to four control isolates consisting of all available serogroup C isolates from Maryland residents with invasive meningococcal disease reported in 1999.



Patterns on pulsed-field gel electrophoresis of *Neisseria meningitidis* restricted by *Spe*I. Lanes 1, 6, 10: lambda ladder reference. Lanes 2, 3, 4: *N meningitidis* isolates from Cases 1, 2, and 3, respectively. Lanes 5, 7, 8, 9: *N meningitidis* control isolates from 1999.

The three case patients had all been previously healthy and had not attended college. A search for a common exposure among the three revealed that all had attended a party on May 14, 1999, which was also attended by at least 80 other persons, most of whom were 18 to 24 years old. At the party, a large number of persons reportedly smoked tobacco, smoked marijuana, and/or drank alcohol. The only exposure common to all three patients was the party. Although the patients in case 1 and case 2 were household roommates, the patient in case 3 had no contact with the other two, either before or after the party. Antimicrobial chemoprophylaxis was recommended to a total of 83 party, work, and household contacts of the patients.

All three isolates from the case patients were confirmed to be *N meningitidis,* and all were serogroup C. The three isolates had identical molecular subtypes with *Spe*I (Figure), *Nhe*I, and *Sfi*I. The four control isolates were clearly different from the three cases and noticeably different from each other.

DISCUSSION

The results of this study show that the three patients with *N meningitidis* had infection caused by the same strain. Pulsed-field gel electrophoresis is a robust tool for determining genetic relatedness among strains and is capable of detecting small differences, including identifying subclones of the same multilocus electrophoretic enzyme type, another method commonly used to subtype *N meningitidis.*[8,9] The control isolates were all different from each other and from the three cases. Although we cannot say with certainty where these patients acquired *N meningitidis,* the epidemiologic investigation suggests that transmission occurred at the May 14 party.

Although meningococcal infection in college students has recently received much attention, meningococcal incidence has substantially increased among high-school-aged adolescents and young adults in the United States.[3,5,10,11] In a recent study in Maryland, the highest incidence in adolescents and young adults was found to be in 17-year-olds, none of whom were in college.[3]

The mechanism for the increased incidence in meningococcal disease in adolescents and young adults is not clear.[12] A shift in age distribution to older children is a hallmark of meningococcal outbreaks,[13] which are generally due to a single strain of *N meningitidis*.[9,14] A similar increase that occurred in Oregon was mostly due to a clone of serogroup B *N meningitidis*.[10] Whether the clone of serogroup C meningococcus that caused our cluster is responsible for the large increase in meningococcal infection in adolescents and adults in Maryland is unknown and is the subject of ongoing investigations.

Traditional risk factors for invasive meningococcal infection include upper respiratory tract infections[15-17] and crowding.[18,19] More recently, bar patronage,[20,21] binge drinking, and passive and active smoking[22,23] have been identified as risk factors for meningococcal infection. Cigarette smoke may increase the risk of meningococcal carriage and invasive disease by disrupting the respiratory epithelium.[24] The increased risk of invasive meningococcal disease associated with bar patronage is thought to be due to a combination of factors that could facilitate transmission, including crowding, poor ventilation, active and passive smoking, smoking-associated coughing, and the sharing of drinking glasses and cigarettes. The party attended by our three patients provided an environment similar to that of a crowded, smoke-filled bar.

In summary, this report of a cluster of meningococcal infection associated with a large party underscores the need for a clearer understanding of the increasing meningococcal incidence in adolescents and young adults. Until recently, the prevalence of smoking among adolescents and young adults had been on the decline. However, over the past few years, these trends are reversing.[25,26] In combination with the recent identification of smoking and drinking as important risk factors for infection in this age group, these trends suggest that at least part of the increase may be due to these potentially modifiable behaviors. Like most meningococcal infection in this age group, cases such as these could potentially be prevented with the tetravalent meningococcal polysaccharide vaccine. Studies to identify risk factors for meningococcal infection in this age group are needed.

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References

1. Schuchat A, Robinson K, Wenger JD, et al: Bacterial meningitis in United States in 1995. *N Engl J Med* 1997; 337:970-976
2. Jackson LA, Wenger JD: Laboratory-based surveillance for meningococcal disease in selected areas, United States, 1989-1991. *MMWR Morb Mortal Wkly Rep* 1993; 42:21-30
3. Harrison LH, Dwyer DM, Maples CT, et al: Risk of meningococcal infection in college students. *JAMA* 1999; 281:1906-1910
4. Rosenstein NE, Perkins BA, Stephens DS, et al: The changing epidemiology of meningococcal disease in the United States, 1992-1996. *J Infect Dis* 1999; 180:1894-1901
5. Harrison LH, Pass MA, Mendelsohn AB, et al: Invasive meningococcal disease in adolescents and young adults. *JAMA* 2001; 286:694-699
6. Knapp JS, Koumans EH: *Neisseria* and *Branhamella*. *Manual of Clinical Microbiology*. Murray PR, Baron EJ, Efaller MA, et al (eds). Washington, DC, American Society for Microbiology, 7th Ed, 1999, pp 586-604
7. Bygraves JA, Maiden MC: Analysis of the clonal relationships between strains of *Neisseria meningitidis* by pulsed field gel electrophoresis. *J Gen Microbiol* 1992; 138:523-531
8. Strathdee CA, Tyler J, Ryan WM, et al: Genomic fingerprinting of *Neisseria meningitidis* associated with group C meningococcal disease in Canada. *J Clin Microbiol* 1993; 31:2506-2508
9. Edmond MB, Hollis RJ, Houston HA, et al: Molecular epidemiology of an outbreak of meningococcal disease in a university community. *J Clin Microbiol* 1995; 33:2209-2211
10. Diermayer M, Hedberg K, Hoesly F, et al: Epidemic in serogroup B meningococcal disease in Oregon: the evolving epidemiology of the ET-5 strain. *JAMA* 1999; 281:1493-1497
11. Bruce MG, Rosenstein NE, Capparella JM, et al: Risk factors for meningococcal disease in college students. *JAMA* 2001; 286:688-693
12. Harrison LH: Preventing meningococcal infection in college students (Editorial). *Clin Infect Dis* 2000; 30:648-651
13. Peltola H, Kataja JM, Makela PH: Shift in the age-distribution of meningococcal disease as predictor of an epidemic? *Lancet* 1982; 2:595-597
14. Moore PS: Meningococcal meningitis in Sub-Saharan Africa: a model for the epidemic process. *Clin Infect Dis* 1992; 14:515-525
15. Moore PS, Hierholzer H, DeWitt W, et al: Respiratory viruses and mycoplasma as cofactors for epidemic group A meningococcal meningitis. *JAMA* 1990; 264:1271-1275
16. Young LS, LaForce FM, Head JJ, et al: A simultaneous outbreak of meningococcal and influenza infections. *N Engl J Med* 1972; 287:5-9
17. Harrison LH, Armstrong CW, Jenkins SR, et al: A cluster of meningococcal disease on a school bus following epidemic influenza. *Arch Intern Med* 1991; 151:1005-1009
18. Thomas JC, Bendana NS, Waterman AH, et al: Risk factors for carriage of meningococcus in the Los Angeles County men's jail system. *Am J Epidemiol* 1991; 133:286-295
19. Tappero J, Reporter R, Wenger JD, et al: Meningococcal disease in Los Angeles County, California, and among men in the county jails. *N Engl J Med* 1996; 335:833-840
20. Imrey PB, Jackson LA, Ludwinski PH, et al: Meningococcal carriage, alcohol consumption, and campus bar patronage in a serogroup C meningococcal disease outbreak. *J Clin Microbiol* 1995; 33:3133-3137
21. Imrey PB, Jackson LA, Ludwinski PH, et al: Outbreak of serogroup C meningococcal disease associated with campus bar patronage. *Am J Epidemiol* 1996; 143:624-630
22. Fischer M, Hedberg K, Cardosi P, et al: Tobacco smoke as a risk factor for meningococcal disease. *Pediatr Infect Dis J* 1997; 16:979-983
23. Stuart JM, Cartwright KA, Robinson PM, et al: Effect of smoking on meningococcal carriage. *Lancet* 1989; 2:723-725
24. Dye JA, Adler KB: Effects of cigarette smoke on epithelial cells of the respiratory tract. *Thorax* 1994; 49:825-834
25. Wechsler H, Rigotti NA, Gledhill-Hoyt J, et al: Increased levels of cigarette use among college students: a cause for national concern. *JAMA* 1998; 280:1673-1678
26. Cigarette smoking among high school students—11 states, 1991-1997. *MMWR Morbid Mortal Wkly Rep* 1999; 48:686-692